REMARKS

Claims 1, 2, 9 to 31, 37 to 39, 41 to 60, 62 to 66, 81, and 86 are currently pending in the instant application. Claims 67 to 79, 80, and 82 to 85 have been withdrawn. Claims 3 to 8, 32 to 36, 40, and 61 have been cancelled without prejudice or disclaimer.

Claim 1 has been amended to recite in relevant part "[a] method for treating a mammal infected with respiratory syncytial virus (RSV)." Claim 1 has also been amended to recite in relevant part that "A, together with the atoms to which it is attached, forms an optionally substituted pyridyl ring;" that "R^1 is selected from $-(CH_2)_nC_{3-7}$ cycloalkyl, $-(CH_2)_nC_{4-7}$ cycloalkenyl, $-(CH_2)_n$ aryl, $-(CH_2)_n$ arylC_{1-12} alkyl, $-(CH_2)_n$ arylC_{2-12} alkenyl, $-(CH_2)_n$ arylC_{2-12} alkynyl and $-(CH_2)_n$ heterocyclyl;" and that X and Y are independently selected from O or S." Support can be found, *e.g.*, in paragraphs [0344] to [0363], and Tables 6 to 10, and claims 1 and 8 of the specification as filed originally.

Claim 24 has been amended to recite in relevant part that "X is oxygen." Support can be found, *e.g.*, in paragraph [0065] of the specification as filed originally.

Claim 30 has been amended to recite in relevant part that "[a] method for the treatment of infections involving RSV." Support can be found, *e.g.*, in paragraphs [0344] to [0363] and Tables 6 to 10 of the specification as filed originally.

Claim 37 has been amended by deleting the term "human metapneumovirus" from the claim, without prejudice or disclaimer.

Claim 38 has been amended by adding the proviso that "R_2 is not unsubstituted $-C_{1-6}$ alkyl." Support can be found, *e.g.*, in paragraph [0072] of the specification as filed originally.

Claim 86 has been amended by adding the proviso that "R_2 is not unsubstituted $-C_{1-6}$ alkyl." Support can be found, *e.g.*, in paragraph [0072] of the specification as filed originally. Claim 86 has also been amended to correct an obvious typographical error by replacing "m is 0, 1, or 2" with "w is 0, 1, or 2."

Claims 9, 10, 12, 39, 63, 68 to 74, and 77 have been amended solely for clarity or for correcting some obvious typographical errors.

Applicants reserve the right to pursue the subject matter of unclaimed subject matter in

the instant application in one or more divisional, continuation, and/or continuation in part applications. Applicants submit that the instant claims are fully supported by the specification as filed originally, and no new matter has been introduced.

A. <u>The Rejection under 35 U.S.C. § 112, First Paragraph, against Claim 34 Should Be Withdrawn</u>

In the May 26, 2010 Office Action, claim 34 is rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully disagree. Nonetheless, solely to expedite the prosecution of the instant application, claim 34 has been cancelled without prejudice or disclaimer, thus rendering the rejection moot. Therefore, Applicants respectfully request that the rejection be withdrawn.

B. <u>The Rejection under 35 U.S.C. § 112, First Paragraph, against Claims 1, 2, 5 to 31, and 35 to 37 Should Be Withdrawn</u>

In the Office Action, claims 1, 2, 5 to 31, and 35 to 37 are rejected under 35 U.S.C. §112, first paragraph, allegedly for lack of enablement for some compounds of Formula I. The rejection is hereby respectfully traversed.

In making an enablement rejection, the Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. *In re Wright,* 999 F.2d 1557, 1562 (Fed. Cir. 1993). Furthermore, a "specification disclosure which contains a teaching of the manner and process of making and using an invention…must be taken as being in compliance with the enablement requirement…unless there is a reason to doubt the objective truth of the statement contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971). "It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224.

In the instant case, besides the conclusory statements in the Office Action (*see,* page 4, lines 14 to page 5, line 3), the Office Action fails to provide any acceptable evidence or sound reasoning as to why claims 1, 2, 5 to 31, and 35 to 37 are not adequately enabled by the instant

disclosure. Contrary to the Examiner's assertion that "the application lack sufficient working examples, guidance, or direction for supporting the scope of compounds defined by general formula I," instant claims 1, 2, 5 to 31, and 35 to 37 are enabled by the specification as originally filed. Evidence in supporting the enablement of these claims can be found, *e.g.,* in paragraphs [0176] to [0261] and [0264] to [0343], and Tables 1 to 3 of the original specification, which discloses sixteen different methods for preparing the compounds of Formula I, and discloses over 500 specific compounds, each characterized at least by MS. Evidence can also be found, *e.g.,* in paragraphs [0344] to [0356], and Tables 6 to 9 of the original specification, which discloses two RSV assays for measuring antiviral activity of the compounds of Formula I, and reports the antiviral activity for over 150 compounds disclosed therein, showing that all the compounds tested are active against RSV with an EC_{50} of no greater than 2,250 ng/mL. Additional evidence can be found, *e.g.*, in paragraphs [0357] to [0360], and Tables 10 and 11 of the original specification, which discloses two animal models for evaluating *in vivo* antiviral activity of the compounds of Formula I, and reports the antiviral activity for selected compounds disclosed therein, showing that all the compounds tested are effective against RSV. With the teachings of the instant application, a skilled artisan at the time of the filing of the instant application would have been able to carry out, without undue experimentation, to make the compounds and test them for activity in order to practice the full scope of the instant claims. Thus, Applicants respectfully submit that the instantly claimed invention is fully enabled by the original specification.

Even assuming, *arguendo*, the Office Action has properly established the enablement rejection, the scope of the instant claims enabled by the instant specification is still much broader than that acknowledged by the Office Action. The Office Action acknowledges that the instant claims are enabled for "treating the viral infection with compound [sic] defined by formula I, wherein A is prydiyl [sic], R1 is a phenyl or substituted phenyl, and R2 is COR3 wherein R3 is optionally substituted aryl, X is oxygen." *See*, Item 8 on page 3 of the Office Action. However, even the scope of the specific compounds disclosed in the instant application is much larger than that acknowledged by the Office Action. For example, R_2 is not just limited to COR_3. Compounds 123, 337, 339, 342, 345, 350, 354, 356, 362, 374 in Table 3 are nonlimiting examples for $R_2 = –COR_3$, where R_3 is alkyl. Compounds 341, 343, 346, 348, 349, 351, 371, 373 in Table 3 are nonlimiting examples for $R_2 = –COR_3$, where R_3 is $–(CH_2)_m$ aryl. Compounds 364 to 370, 375 to 492, in Table 3 are nonlimiting examples for $R_2 = –COR_3$, where R_3 is $–(CH_2)_m$

heterocyclyl. Compounds 493 to 497 in Table 3 are nonlimiting examples for $R_2 = -CH_2R_3$. Compounds 493 to 497 in Table 3 are nonlimiting examples for $R_2 = -CH_2R_3$. Compounds 498 to 501 in Table 3 are examples for $R_2 = -C(Y)N(R_4)R_3$. Compound 502 is a nonlimiting example for $R_2 = -S(O)_wR_5$.

Nonetheless, solely to expedite prosecution, and without prejudice or disclaimers, instant claim 1 has been amended to recite "a method of treating a mammal infected with respiratory syncytial virus (RSV)," and to recite that "R^1 is selected from $-(CH_2)_nC_{3-7}$ cycloalkyl, $-(CH_2)_nC_{4-7}$ cycloalkenyl, $-(CH_2)_n$ aryl, $-(CH_2)_n$ arylC_{1-12} alkyl, $-(CH_2)_n$ arylC_{2-12} alkenyl, $-(CH_2)_n$ arylC_{2-12} alkynyl and $-(CH_2)_n$ heterocyclyl;" and "X and Y are independently selected from O or S." Therefore, Applicants respectfully request that this rejection be withdrawn.

C. <u>The Rejection under 35 U.S.C. § 102(b) against Claims 38, 39, 43, 50 to 60, and 86 Should Be Withdrawn</u>

In the Office Action, claims 38, 39, 43, 50 to 60, and 86 are rejected under 35 U.S.C. §102(b), allegedly as being anticipated by Sulkowski *et al.* (US 3,311,629). The rejection is hereby respectfully traversed.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628 (Fed. Cir. 1987).

In the instant application, independent claim 38 as amended herein and its dependent claims 39, 43, and 50 to 60, and independent claim 86 as amended herein are directed toward a compound of Formula I, wherein "R_2 is not unsubstituted $-C_{1-6}$ alkyl." However, Sulkowski *et al.* fail to teach any specific compounds that fall within the scope of any of these claims, and thus fail to teach each and every element of the claims and cannot anticipate the claims. Therefore, Applicants respectfully request that this rejection be withdrawn.

D. <u>The Rejection under 35 U.S.C. § 103(a) against Claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 Should Be Withdrawn</u>

In the Office Action, claims 33, 38, 39, 41 to 60, 62 to 66, 81, and 86 are rejected under 35 U.S.C. §103(a), allegedly as being unpatentable over Bamba *et al.* (WO 02/066479, "the '479 publication"). The rejection is hereby respectfully traversed.

"The determination of obviousness is a matter of law based on findings of underlying fact, wherein the factors identified in *Graham v. John Deere Co.*, . . . guide the inquiry . . . ." *Sanofi-Synthelabo, Inc. v. Apotex, Inc.*, 550 F.3d 1075, 1085 (Fed. Cir. 2008), citing *Graham v. John Deere Co.*, 383 U.S. 1 (1966); *see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 399 (2007). The factors identified in *Graham* are: (1) "the scope and content of the prior art;" (2) "the differences between the prior art and the claims;" (3) "the level of ordinary skill in the pertinent art;" and (4) "secondary considerations." *Graham*, 383 U.S. at 17–18. "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 401. It is important to identify "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.*

To establish a *prima facie* case of obviousness of new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). Furthermore, support for a proper *prima facie* case of obviousness of a new compound based on structural similarity of a prior art compound requires the identification of a reason as to why one of ordinary skill in the art would *select* and *modify* a known compound in a particular way to achieve the claimed compound. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008) (emphasis added). Even in light of *KSR*, the Federal Circuit has maintained that the chemical arts are often unpredictable, such that *KSR*'s focus on "identified predictable solutions" may present a difficult hurdle to overcome because potential solutions in the chemical arts are less likely to be genuinely predictable. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, in order to establish a proper *prima facie* case of obviousness based on structural similarity, the Examiner must identify: (1) why one of ordinary skill in the art would have selected a particular compound from the cited reference as a lead compound; and (2) why one of ordinary skill in the art would have modified that particular compound in a particular way to arrive at the instantly claimed compounds. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008).

The Office Action fails to establish a *prima facie* case of obviousness. The instant claims are directed toward compounds that are useful in treating RSV infections and methods for treating RSV infections. However, Bamba *et al.* disclose compounds for treating diabetes. *See*, the English abstract of the '479 publication. Bamba *et al.* are completely silent as to the

treatment of viral infections, let alone the treatment of RSV infections. *See*, the English abstract of the '479 publication.

Furthermore, the Office Action fails to provide any reason as why one of ordinary skill in the art would have been motivated to select any of the compounds disclosed in Bamba *et al.*, which had not been shown to be active against RSV at the time of its disclosure, as a lead to develop the instantly claimed compounds and methods for the treatment of RSV infections. The Office Action also fails to provide any reason as why one of ordinary skill in the art would have been motivated to modify any particular compound disclosed in Bamba *et al.* in a particular way to arrive at the instantly claimed compounds.

The chemical arts are often unpredictable, and the modification of a lead compound often leads to different activity. *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996 (Fed. Cir. 2009). Thus, without the teaching of the instant application, one skilled in the art would have no reasonable expectation from the disclosure of Bamba *et al.* that the instant compounds could be active against RSV and useful for treating RSV infections. In this regard, the Office Action is impermissibly using hindsight reconstruction in its allegation of obviousness.

Therefore, the instant claims are not *prima facie* obvious, and reconsideration and withdrawal of the rejection are respectfully requested.

SUMMARY

Should the Examiner believe that prosecution of this application might be expedited by further discussion of any remaining issue, the Examiner is cordially invited to contact the undersigned representative of Applicants, Dale L. Rieger, Ph.D., by phone at (858) 314-1200 or by email at drieger@jonesday.com.

The United States Patent and Trademark Office is hereby authorized to charge the fee for one-month extension of time under 37 C.F.R. § 1.136(a), which will be paid via EFS. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-3013 and please credit any excess fees to such deposit account.

Respectfully submitted,

Dated: September 22, 2010

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